PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
JANE MASSEY LICATA
LICATA & TYRRELL PC
66E. MAIN STREET
MARLTON, NJ 08053

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	21 JAN 2005
Applicant's or agent's file reference WSTR-0017C	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US04/00899	14 January 2004 (14.01.2004)	16 January 2003 (16.01.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 39/145, 39/38, 39/12, 39/385, 39/285; C07K 17/00, 16/00 and US Cl.: 424/206.1, 210.1, 184.1, 186.1, 194.1, 196.11, 201.1; 530/350, 388.3

Applicant

THE WISTAR INSTITUTE

1. This opinion contains indications relating to the following items:

- [x] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [x] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [ ] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Michael M. McGaw Telephone No. 571-272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/00899

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language ____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/00899

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims NONE	YES
	Claims 1-4, 6	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-15	NO
Industrial applicability (IA)	Claims 1-15	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-4 and 6 lack novelty under PCT Article 33(2) as being anticipated by Kragol, G. et al. (2001) Bioorganic and Medicinal Chemistry Letters, 11:1417-1420.

Kragol et al. teach a multiple antigenic agent as claimed in claim 1. See particularly "Scheme 1" on page 1418. The multiple antigenic agent taught by Kragol included B cell and T-cell determinants from influenza A virus. See page 1814, col. 1. The B cell determinant was from the ectodomain of the M2 protein. The T cell determinants were the S1 and S2 T-helper cell epitopes from the hemagglutinin protein.

Claims 5 and 7-15 lack an inventive step under PCT Article 33(3) as being obvious over Kragol, G. et al. (2001) Bioorganic and Medicinal Chemistry Letters, 11:1417-1420 in view of Nierynck, S. et al. (1999).

Kragol, G. et al. (2001) is as described above. Nierynck, S. et al. (1999) teach a universal influenza A vaccine based on the extracellular domain of the M2 protein. Nierynck used the ectodomain of the M2 protein fused to the N-terminal portion of the hepatitis B virus core protein as a vaccine against influenza. The vaccine was administered to mice with Ribi adjuvant. See page 1162, col. 2. The vaccine protected mice from lethal challenge using both heterologous and homologous influenza A. See table 3, page 1160.